I hereby certify that this correspondence is being deposited with the United States
Postal Service as Express mail in an envelope addressed to:
Assistant Commissioner for Patents,
Washington, D.C. 20231,
On______September 12, 2001

The Law Offices of Jonathan Alan Quine

Tracie Brooks

31050 U.S. PTO 09/954692 09/12/01

Attorney Docket No. 02-020522US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Phillip A. Patten, et al.

Application No.: Not yet known

Filed:

For: METHODS AND COMPOSITIONS FOR POLYPEPTIDE ENGINEERING

Examiner: Unassigned

Art Unit: Unassigned

INFORMATION DISCLOSURE STATEMENT UNDER 37 CFR § 1.97 and

§ 1.98

Assistant Commissioner for Patents Washington, D.C. 20231

Sir:

The references cited on attached PTO-1449 and 892 forms are being called to the attention of the Examiner to make of record references cited in parent application USSN 08/769,062 filed December 18, 1996. Pursuant to 37 CFR § 1.98(d), copies of references cited in parent application USSN 08/769,062 filed December 18, 1996 are not provided. Copy of 1449's from USSN 08/621,859 filed March 25, 1996 are included as well, as they were submitted in the parent application. However the applicants will gladly provided fresh copies of any references requested by the Examiner. It is respectfully requested that the cited

Application No.: Not yet known Page 2

information on the previously submitted 1449 and 892 forms for application USSN 08/769,062 filed December 18, 1996 be expressly considered during the prosecution of this application, and that references be made of record therein and appear among the "references cited" on any patent to issue therefrom.

As provided for by 37 CFR 1.97(g) and (h), no inference should be made that the information and references cited are prior art merely because they are in this statement and no representation is being made that a search has been conducted or that this statement encompasses all the possible relevant information.

Applicant believes that <u>no fee is required</u> for submission of this statement, since it is being submitted prior to the first Office Action. However, if a fee is required, the Commissioner is authorized to deduct such fee from the undersigned's Deposit Account No. 50-0893. Please deduct any additional fees from, or credit any overpayment to, the above-noted Deposit Account.

Respectfully submitted,

Christopher C. Sappenfield

W (Apl D)

Reg. No. 45,073

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Substitute for form 1449A-B/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

COPY FROM PARENT

(use as many sheets as necessary)

C	omplete if Known
Application Number	-09/717419 Unassigned
Filing Date	November 18, 2000 massigned
First Named Inventor	Phillip A. Patten
Group Art Unit	1634
Examiner Name	S. Zitomer
Attorney Docket Number	12-020520US OZ-020522US

			U.	S. PATENT DOCUMENTS		
		U.S. Patent Do		Name of Patentee or Applicant of	Date of Publication of	Pages, Columns, lines,
Examiner Initials	Cite No.	Number	Kind Code (if known)	Cited Document	Cited Document MM-DD-YYYY	Where Relevant Passages or Relevant Figures Appeal
	AA	5,427,930		Birkenmeyer et al.	06-27-1995	
	AB	5,792,607		Backman et al.	08-11-1998	ra
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Examiner Initials	Cite No.	Office	Number	Kind Code (if known)	Name of Patentee or Applicant of Cited Document	of Cited Document MM-DD-YYYY	Where Relevant Passages or Relevant Figures Appear	1
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·		OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS	
Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	т

Examiner	•	Date	
Signature		Considered	

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

C	Complete if Known
Application Number	109/717419 massigned
Filing Date	November 18, 2000 Unassaved
First Named Inventor	Phillip A. Patten
Group Art Unit	Unassigned
Examiner Name	Unassigned
Attorney Docket Number	02-020520US 02-020522US

			U.	S. PATENT DOCUMENTS		
Examiner Initials	Cite No.	U.S. Patent Di Number	Kind Code (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, lines, Where Relevant Passages or Relevant Figures Appeal
	AA	6,596,548		Stemmer	08-01-2000	
	AB	6,117,679		Stemmer	09-12-2000	
	AC	6,132,970		Stemmer	10-17-2000	

				FOREIG	N PATENT DOCUMEN	TS		
Examiner Initials	Cite No.	Office	Foreign Patent Docu	Kind Code (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	Т
	AD	wo	98/42832		Cal Tech	10-01-1998		
	AE	wo	98/41653		Novo Nordisk	09-24-1998		
	AF	wo	99/29902		Cal Tech	06-17-1999		

		OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS	
Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T
	AG	CARTER, "Improved Oligonucleotide-Directed Mutagenesis Using M13 Vectors," Methods in Enzymology, 154:382 (1987)	
	AH	KRAMER AND FRITZ, "Oligonucleotide-Directed Construction of Mutations via Gapped Duplex DNA," Methods in Enzymology, 154:350-367 (1987).	
;	Al	KUNKEL, "Rapid and efficient site-specific mutagenesis without phenotypic selection," PNAS, 82:488-492 (Jan. 1985).	
	AJ	KUNKEL et al., "Rapid and Efficient Site-Specific Mutagenesis without Phenotypic Selection," Methods in Enzymology, 154:367-382 (1987).	
	AK	ZOLLER AND SMITH, "Oligonucleotide-Directed Mutagenesis: A Simple Method using Two Oligonucleotide Primers and a Single-Stranded DNA Template," Methods in Enzymology, 154:329 (1987).	
:	AL	PRODROMOU et al., (1992) "Recursive PCR: a novel technique for total gene synthesis." Protein Engineering 5(8): 827-829.	
	AM	Statutory Declaration signed by Ruth Bird as filed in pending Australian opposition case, Australian Application No. 703264.	
	AN	Statutory Declaration signed by Ngaire Pettit-Young as filed in pending Australian opposition case, Australian Application No. 703264	
	AO	Statutory Declaration signed by Mae Li Gan as filed in pending Australian opposition case, Australian Application No. 703264.	

Examiner	Date	
Signature	Considered	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

COPY FROM PARENT

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C	omplete if Known
Application Number	-09/717418 unassaned
Filing Date	November 18, 2000 Unassign och
First Named Inventor	Phillip A. Patten
Group Art Unit	Unassigned Q
Examiner Name	Unassigned
Attorney Docket Number	102-020520US 02-020522USW.

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AP	HIGUCHI et al., (1988) "A genaral method of <i>in vitro</i> preparation and specific mutagensis of DNA fragments: study of protein and DNA interactions." <u>Nucleis Acids Research</u> 16(15): 7351-7367.	11050
AQ	SHI et al., (1993) "Rapid PCR Construction of a Gene Containing Lym-1 Antibody Variable Regions." PCR Methods and Applications 3: 46-53.	
 AR	SHULDINER, A.R. et al., (1989) "Hybrid DNA artifact from PCR of closely related target sequences," <i>Nuc. Acids Res.</i> 17(11): 4409.	
 AS	SANDHU, G.S. et al., (1992) "Dual Asymmetric PCR: One-Step Construction of Synthetic Genes," <i>Biotechniques</i> 12(01): 14-16.	
AT	Biotransformations, Pathogenesis, and Evolving Biotechnology, Program and Abstracts, Pseudomonas '89, American Society for Microbiology and The University of Illinois, July 9-13, 1989, Abstract Nos. 11-21 – 11-25, p. 26.	
AU	SMITH et al. (1991) "Losalized sex in bacteria," Nature, 349: 29-31.	
 AV	MICHAEL et al., (c. 1997) "Thermostable Ligase-Mediated Incorporation of Mutagenic Oligonucleotides During PCR Amplifications," <i>Methods in Molecular Biology</i> , Vol. 67, PCR Cloning Protocals: From Molecular Colning to Genetic Engineering pp. 189-195.	
 AW	NER et al. (1988) "Laboratory Methods: A Simple and Efficient Procedure for Generating Random Point Mutations and for Codon Replacements Using Mixed Oligodeoxynucleotides," DNA 7: 127-134.	
AX	MERYHANS et al., (1990) "DNA recombination during PCR," Nuc Acids Res. 18(7): 1687-1691.	
AY	WEBBER et al. (1983) "Formation of gene coding for hybrid proteins by recombination between related cloned genes in <i>E. coli.</i> " <i>Nuc. Acids Res.</i> 11(16): 5661-5669.	
 AZ	POMPON et al. (1989) "Protein engineering by cDNA recombination in yeasts, shuffling of mammalian cytochrome P-450 functions." <i>Gene</i> 83: 15-24.	
 ВА	HORTON et al. (1990) "Gene splicing by overlap extension: Tailor-made genes using the polymerase chain reaction." <i>Biotechniques</i> 8(5): 528-535.	
 BB	KLUG et al. (1991) "Creating chimeric molecules by PCR directed homologous DNA recombination." <i>Nuc. Acids Res.</i> 19(10): 2793.	
ВС	ROUWENDAL et al., (1993) "Simultaneous Mutagenesis of Multiple Sites: Application of the Ugase Chain Reaction Using PCR Products instead of Oligonucleotides." <i>Biotechniques</i> 15(1): 68-70, 72-74, 76.	

Examiner	Date	
Signature	Considered	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

C	omplete if Known
Application Number	-00/709,002 Unassigned,
Filing Date	December 18, 1996 Unassigned
First Named Inventor	Phillip A. Patten
Group Art Unit	1634
Examiner Name	Zitomer, S.
Attorney Docket Number	-02-020500UG 02-020522US

		U.S. Patent Do		S. PATENT DOCUMEN Name of Patentee or Applicant	of Date of Publication of	Pages, Columns, lines,
Examiner Initials	Cite No.	Number	Kind Code (if known)	Cited Document	Cited Document MM-DD-YYYY	Where Relevant Passages or Relevant Figures Appea
	AA	4,766,106		Katre et al.	08-23-1988	
	AB	4,795,699		Tabor et al.	01-03-1989	⁶ 2
	ΔΛ	4.816.567		Cahilly of al	03_28_1080	s. 469
	AD	4,902,502		Nitecki et al.	02-20-1990	, c
	AE	5,264,563		Huse	11-23-1993	000
	AF	5,314,809		Erlich et al.	05-24-1994	31
	AG	5,512,463		Stemmer	04-30-1996	
-	AH	5,514,568		Stemmer	05-07-1996	
	Al	5,514,588		Varadaraj	05-07-1996	
	AJ	5,523,388		Huse	06-04-1996	
	AK	5,541,311		Dahlberg et al.	07-30-1996	
	AL	5,547,859		Goodman et al.	08-20-1996	·
	AM	5,574,205		Kucherlapati et al.	11-12-1996	
	AN	5,667,974		Birkenmeyer et al.	09-16-1997	
	AO	5,698,426		Huse	12-16-1997	
	AP	5,756,316		Schellenberger	05-26-1998	
	AQ	5,770,434		Huse	06-23-1998	
	AR	5,808,022		Huse	09-15-1998	
	AS	5,824,496		Horwitz et al.	10-20-1998	
	AT	5,830,696		Short	11-03-1998	
	AU	5,843,643		Ratner	12-01-1998	
	AV	5,858,725		Crowe	01-12-1999	
	AW	5,866,363		Pieczenic	02-02-1999	
	AX	5,871,974		Huse	02-16-1999	
	AY	5,877,402		Maliga et al.	03-02-1999	
<u> </u>	AZ	5,885,813		Davis et al.	03-23-1999	
	ВА	5,928,905		Stemmer et al.	07-27-1999	
xamine Signatur	1	1		1	Date Considered	

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.



INFORMATION DISCLOSURE STATEMENT BY APPLICANT

C	omplete if Known
Application Number	-08/769,062 UNOSSIGNED
Filing Date	December 18, 1996 Unassianed
First Named Inventor	Phillip A. Patten
Group Art Unit	1634
Examiner Name	Zitomer, S.
Attorney Docket Number	-02-020500US 02-020522US

ВВ	5,955,358		Huse	09-21-1999	
ВС	5,965,415		Radman et al.	10-12-1999	
BD	6,001,574		Short	12-14-1999	
BE	6,004,788		Short	12-21-1999	
BF	6,015,694		Dubenskey et al.	01-18-2000	
50	0,000,770	1	onort	02-29-2000	
ВН	6,051,049		Hansen et al.	04-18-2000	
ВІ	6,054,267		Short	04-25-2000	
BJ	6,057,103		Short	05-02-2000	
ВК	6,071,889		Weiss et al.	06-06-2000	
BL	6,074,853		Pati et al.	06-13-2000	
ВМ	6,087,177		Wohlstadter	07-11-2000	
BN	6,093,873		Chambon et al.	07-25-2000	
ВО	6,096,548		Stemmer	08-01-2000	
ВР	6,114,115		Wagner, Jr.	09-05-2000	
BQ	6,117,679		Stemmer	09-12-2000	
BR	6,132,970		Stemmer	10-17-2000	
BS	6,153,410		Arnold et al.	11-28-2000	
ВТ	6,159,687		Vind	12-12-2000	
BU	6,171,820	B1	Short	01-09-2001	
BV	6,174,673	B1	Short et al.	01-16-2001	
BW	6,168,919	B1	Short	01-02-2001	
BX	6,177,263	B1	Arnold et al.	01-23-2001	
BY	5,795,747		Henco	08-18-1998	

				FOREIGI	N PATENT DOCUMEN	TS		
			Foreign Patent Docu	ment		Date of Publication	Pages, Columns, Lines,	_
Examiner Initials	Cite No.	Office	Number	Kind Code (if known)	Name of Patentee or Applicant of Cited Document	of Cited Document MM-DD-YYYY	Where Relevant Passages or Relevant Figures Appear	T
•	BZ	EP	0 544 809	B1	Ixsys, Inc.	12-16-1998		
	CA	EP	0 563 296	B1	lxsys, Inc.	03-17-1999		

Examiner	Date	
Signature	Considered	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

COPY FROM PARENT

С	omplete if Known
Application Number	-08/769,062 Unassigned
Filing Date	December 18, 1996 Unassigned
First Named Inventor	Phillip A. Patten
Group Art Unit	1634
Examiner Name	Zitomer, S.
Attorney Docket Number	02-020500US 02-020522US

	СВ	EP	0 552 266	B1	The Wellcome Foundation LTD.	01-19-2000
	СС	EP	0 397 463	A2	Berlex Laboratories	11-14-1990
	CD	EP	0 397 463	A3	Berlex Laboratories	11-14-1990
	CE	wo	90/14424	A1	Scripps Clinic and	11-29-1990
	1	1			rounuation	
	CF	wo	92/06176	A1	IXSYS, Inc	04-16-1992
	CG	wo	92/18645	A1	Henco	10-29-1992
	СН	wo	93/01282	A1	Berlex Laboratories, Inc.	01-21-1993
	CI	wo	93/18175	A1	Life Technologies, Inc.	09-16-1993
	Cl	wo	93/19172	A1	Cambridge Antibody Technology LTD.	09-30-1993
· · · · · · · · · · · · · · · · · · ·	СК	wo	94/11496	A1	IXSYS, Inc	05-26-1994
	CL	wo	97/46670	A1	Masssachsetts Institute of Technology	12-11-1997
	СМ	wo	99/29902	A1	California Institute of Technology	06-17-1999

		OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS	1
Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	т
	CN	ADEY ET AL. "Preparation of second-generation phage libraries." Proteins 227-291. (1996)	
	со	Berger et al. "Prospective: Expanding the Potantial of Restriction Endonucleases: Use of Hapaxoterministic Enzymes." <i>Anal Biochenistry</i> 222:1-8 (1994)	
	СР	Biotransformations Amer Soc.Abstract no.11-21&11-25 Pg.26 (July 1989)	
	ca	CARTER "Improved Oligonucleotide-Directed Mutagenesis Usinf M13 Vectors." <i>Methods of Enzymology</i> 154:382-403 (1985)	
	CR	COLLET ET AL. "A binary plasmid system for shuffling combinational antibody libraries." <i>Proc. Natl. Acad. Sci. USA</i> 89(21)L10026-10030 (1992)	
,	cs	DANGL ET AL. "Rapid Isloation of Cloned Isotype Switch Variants Using Fluprescent Activated Cell Sorting." Cytometry 2(6):395-401 (1982)	
	СТ	DIERICK ET AL. "Incorporation of dITP of 7-deaza dGTP during PCR improves sequencing of the product." <i>Nuc. Acid Res.</i> 21(18):4427-4428 (1993)	

Examiner Date Signature Considered

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

COPY FROM PARENT

(use as many sheets as necessary)

C	Complete if Known
Application Number	08/789,082 Unassigned
Filing Date	-December 18, 1996 UNASSIGNED
First Named Inventor	Phillip A. Patten
Group Art Unit	1634
Examiner Name	Zitomer, S.
Attorney Docket Number	02-020500U3-02-D2D522US

CU	FULLEN ET AL. "Genetic Algorithms and Recursive Ensemble Mutagenesis in Protein Engineering." Complex.Inrt.94, from website (1992)
CV	HEDA ET AL. "A simple in vitro site directed mutagenesis of concatamerized cDNA by inverse polymerase chain reaction." <i>Nuc. Acids Res.</i> 20(19):5241-5242 (1992)
CW	HIGUCHI ET AL "A general method of in vitro preparation and specific mutagenesis of DNA fragments study of protein and DNA interactions." <i>Nuc. Acids Res.</i> 16(15):7351-7367 (1988)
СХ	HODGSON "The Whys and Wherefores of DNA Amplification." <i>Biotechnology</i> 11(8):940-942
CY	Kang et al. Antibody redesigned by chain shuffling from ramdom combinatorial immunglobulin libraries." Proc. Natl. Acad. Sci. USA 88(24):11120-11123 (1991)
CZ	KLUG ET AL. "Creating chimeric molecules by PCR directed homogous DNA recombination." Nuc Acids.Res. 19(10):2793 (1991)
DA	KOMANO ET AL. "Distribution of Shufflon among Incl Plasmids." J. Bacteriology 169(11):5317-5319. (1987)
DB	KOMANO ET AL. "Physical and Genetic Analysis of Incl2 Plasmid R721: Evidence for the Presence of Shufflon." Plasmid 23:248-251. (1991)
DC	KRAMER & FRITZ "Oligonucleotide-Directed Construction of Mutations via Gapped Duplex DNA." Methods of Enzymology 154:350-367 (1978)
DD	Kunkel "Rapid and Efficient Site-Specific Mutagenesis without Phenotypic Selection." Methods in Enzmology 154:367-382 (1987)
DE	KUNKEL "Rapid and efficient site-specific mutagenesis without phenotype selection." <i>Proc. Matl. Acad. Sci USA</i> 82:488-492 (1985)
DF	LOWNAM ET AL. "Affiniy Maturation of Human Growth Hormone by Monavalent Phage Display." J. Mol. Biol. 234:654-578 (1993)
DG	MAJUMDER "Ligation-free gene synthesis by PCR: synthesis and mutagenesis at multiple loci of a chimeric gene encoding OmpA signal peptide and hirudin." Gene 110(1):89-94 (1992)
DH	MERYHANS ET AL. "DNA recombination during PCR." Nuc Acids.Res. 18(7):1687-1691 (1990)
DI	MICHAEL "Thremostable Ligase-Medicated Incorporation of Mutagenic Oligonucleotides During PCR Amplification." <i>Meth. In Mol Biol.</i> 67:189-195 (1997)
DJ	NER ET AL. "Laboratory Methods." DNA 7:127-134 (1988)
DK	OLSEN ET AL. "Hybrid Baccillus (1-3,1-4)-β-glucanases: engineering thermostable enzymes by construction of hybrid genes." Mol. Gen. Genet 225(2):-177-185 (1987)
DL	REIKOFSKI & TAO "Polymerase Chain Reaction (PCR) Techniques for Site-directed Mutagenesis." Biotech Adv. 10:535-547(1992)
DM	ROBLES ET AL."Hydorpathy and Molar Volume Constraints on Combinatorial Mutants of the Photosynthetic Reaction Center." J.Mol.Biol., 232:242-252 (1993)
DN	ROUWENDAL ET AL. "Simultaneous Mutagenesis of Multiple Sites: Application of the Ligase Chain Reaction Using PCR Products Instead of Oligonucleotides." <i>Biotechniques</i> 15(1):68-70, 72-74, 76 (1993)
DO	SANDHU ET AL. "Dual Asymmetric PCR: One-Step Construction of Synthetic Genes." Biotechniques 12)01):14-16 (1992)
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Examiner	Date	
Signature	Considered	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

Complete if Known			
Application Number	-08/769,062 UNOUS 19 Ned		
Filing Date	December 18, 1996 Massigned		
First Named Inventor	Phillip A. Patten		
Group Art Unit	1634		
Examiner Name	Zitomer, S.		
Attorney Docket Number	02 020500US 02-020522US		

DP	SHI ET AL "Rapid PCR Construction of a Gene Cotaining Lym-1 Antibody Variable Regions." PCS Meth. & Appl. 3:46-52 (1993)	
DQ	SHULDINER ET AL. "Hybrid DNA artifact from PCR of closely related target sequences." Nus. Acids Res. 17(11):4409 (1989)	
DR	SMITH ET AL. "Localized sex in Bacteria." Nature 349:29-31 (1991)	
DS	Statutory Declaration by Mae Li Gan No. 703264	
ļ		
DU	Statutory Declaration by Ruth Bird No. 703264	
DV	STEMMER ET AL. "A 20-Minute Ethidium Bromide High-slat Extraction Protocol for Pasmid DNA." Biotechniques 10(6):726 (1991)	
DW	STEMMER ET AL. "Enzymatic Inverse PCR– A Restriction Cite Independent, Single-Fragment Method for High-Efficiency, Site-Directed Mutagenesis." Biotechniques 13(2):214. (1992)	
DX	STEMMER ET AL. (1991) R342 "Expression of Antibody By Fragments Specific for a Heavy Metal Chelate (indium EDTA) in E-Coli." J. Cell Biochem 217	
DY	STEMMER ET AL. "Increased Antibody Expression for Escherichia-Coli Through Wobble-Base Library Mutagenesis by Enzymatic Inverse PCR." Gene 123(1):1-7. (1993)	
DZ	WU ET AL. "Allale-specific enzymatic amplification of β-globin genomis DNA for diagnosis of sickle cell anema." Proc. Natl. Acad. Sci Vol 86:2757-2760. (1999)	
EA	ZOLLER & SMITH "Oligonucleotide-Directed Mutagenesis: A Simple Method using Two Oligonucleotide Primers and a Single-Stranded DNA Template." <i>Methods in Enzymology</i> 154:329-347 (1987)	

Examiner	Date	
Signature	Considered	

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C	omplete if Known , ,
Application Number	108/769,082 Unassaned
Filing Date	Docember 18, 1996 Massigned
First Named Inventor	Phillip A. Patten
Group Art Unit	1634
Examiner Name	Zitomer, S.
Attorney Docket Number	02 020500US 02-0205 22US

	U.S. Patent Document		S. PATENT DOCUMENTS Name of Patentee or Applicant of	Date of Publication of	Pages, Columns, lines,	
Examiner Initials	Cite No.	Number	Kind Code (if known)	Cited Document	Cited Document MM-DD-YYYY	Where Relevant Passages or Relevant Figures Appeal
	AA	5,665,859		Wallach et al.	09-09-1997	0
	AB	5,741,694		Hasrtup et al.	04-21-1998	PT P
	40	5 750 373		Garrard et al	05-12-1998	S. 6
	AD	5,427,930		Birkenmeyer et al.	06-27-1995	n 6/
	ΑE	5,792,607		Backman et al.	08-11-1998	1105

		oreign Patent Docu			Date of Publication	Pages, Columns, Lines,	
Examiner Cite Initials No.	Office	Number	Kind Code (if known)	Name of Patentee or Applicant of Cited Document		Where Relevant Passages or Relevant Figures Appear	
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Application Number	08/769,062 massigned		
Filing Date	Docember 18, 1996 Unbssigned		
First Named Inventor	Phillip A. Patten		
Group Art Unit	1634		
Examiner Name	Zitomer, S.		
	02-020500U3-02-020522US		

	T	U.S. Patent Document		Name of Patentee or Applicant of	Date of Publication of	Pages, Columns, lines.
Examiner Initials	Cite No	Number	Kind Code (if known)	Cited Document	Cited Document MM-DD-YYYY	Where Relevant Passages or Relevant Figures Appear
	АА	4,683,202		Mullis	07-28-1987	от с
	AB	4,800,159		Mullis et al.	01-24-1989	S. F
	AC	4,965,188		Mullis et al.	10-23-1990	5. S
	AD	5,023,171		Но	06-11-1991	00°0 9/9
	AE	5,176,995		Sninsky et al.	01-05-1993	J.10
	AF	5,187,083		Mullis	02-16-1993	
	AG	5,234,824		Mullis	08-10-1993	
	АН	5,502,167		Waldmann	03-26-1996	
	ΑI	5,556,772		Sorge et al.	09-17-1996	
	AJ	5,714,316		Weiner et al.	02-03-1998	
	AK	5,851,813		Desrosiers	12-22-1998	
	AL	5,858,725		Crowe et al.	01-12-1999	

			FOREIG	N PATENT DOCUMEN			,
Cite No.	Office	Foreign Patent Docur	Kind Code (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	Т
AM	wo	90/14430	-	Scripps Clinic & Research Found.	11-29-1990		
AN	wo	91/06570		Univ. of Melbourne	05-16-1991		
AO	wo	92/07075		Wellcome Foundation Ltd.	04-30-1992		
AP	wo	93/02191		Wellcome Foundation Ltd.	02-04-1993		
AQ	wo	93/06213		MRC	04-01-1993		
AR	wo	93/11237		Wellcome Foundation Ltd.	06-10-1993		
AS	wo	93/15208		Genzyme Ltd.	08-05-1993		
AT	wo	93/16192		Wellcome Foundation Ltd.	08-19-1993		
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WO	93/25237	City of Hope	12-23-1993	
wo	94/03596	Univ. of Hawaii	02-17-1994	
wo	94/09817	City of Hope	05-11-1994	
wo	94/13804	Cambridge Antibody Tech. Ltd. Medical Res. Council	06-23-1994	
1	wo	WO 94/03596 WO 94/09817	WO 94/03596 Univ. of Hawaii WO 94/09817 City of Hope WO 94/13804 Cambridge Antibody Tech. Ltd. Medical	WO 94/03596 Univ. of Hawaii 02-17-1994 WO 94/09817 City of Hope 05-11-1994 WO 94/13804 Cambridge Antibody Tech. Ltd. Medical

		OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS	
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	AZ	Delgrave et al., (1993) Bio/Technology 11:1548-1552	-
	ВА	Goldman, E.R. and Youvan D.C., (1992) Bio/Technology 10:1557-1561	1
- 41	вв	Joyce, G.F., (1992) Scientific American, December, 90-97	1-
	вс	Bock, L.C., et al., (1992) Nature <u>355</u> :564-566	<u> </u>
-	BD	Scott, J.K. and Smith G.P., (1990) Science <u>249</u> :386-390	<u> </u>
	BE	Cwirla, S.E. et al.,(1990) Proc Nat'l Acad Sci USA 87:6378-6382	-
	BF	McCafferty, J. et al., (1990) Nature <u>348</u> :552-554	_
	BG	Cull, M.G. et al.,(1992) Proc Natl Acad Sci USA 89:1865-1869	_
	ВН	Nissim et al., (1994) ENBO J <u>13</u> :692-698	-
	ВІ	Krishnan et al., (1991)Nucleic Acids Res. <u>19</u> (22):6177-6182	
	ВЈ	Klug et al., (1991) Nucleic Acids Res. <u>19</u> (10):2793	
	ВК	Daugherty et al., (1991) Nucleic Acids Res. <u>19</u> :2471-2476	_
	BL	Yolov et al. (1990) Nucleic Acids Res. <u>18</u> :3983-3986	1
	ВМ	Jayaraman et al. (1991) Proc Natl Acad Sci USA 88:4084-4088	-
	BN	Morl, M and Schmelzer, C. (1990) Nucleic Acids Res. <u>18</u> (22):6545-6551	\perp
	во	Mullis et al., (1986) Cold Harbor Spring Symposia on Quantitative Biology 51:263-273	
	ВР	Sikorski et al., (1991) Methods in Enzymology 194:302-318	_
	BQ	Mullis et al., (1987) Methods in Enzymology 155:335-350	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT COPY FROM PARENT

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Application Number	08/769,062 massaned
Filing Date	December 18, 1996 Massigned
First Named Inventor	Phillip A. Patten
Group Art Unit	1634
Examiner Name	Zitomer, S.
Attorney Docket Number	-02-020500US - 02-020522US

	BR	Scharf et al., (1986) Science <u>233</u> :1076-1078
	BS	Saiki et al., (1988) Science 239:487-491
	вт	Saiki et al., (1986) Nature <u>324</u> (13):163-166
	BU	Saiki et al., (1985) Science <u>230</u> :1350-1354
	BV	Saiki et al., (1988) New Eng J Med <u>319</u> (9):537-541
	BW	Crameri et al., (1993) Nucleic Acids Res. <u>21</u> (18):4410
	вх	Villareal XC et al., (1991) Anal Biochem. <u>197</u> (2)362-367
	BY	Jones et al., (1991) <i>Biotechniques</i> <u>10</u> (1):62-66
	BZ	Weissenhorn et al., (1991) Gene 106(2):273-277
	CA	Majumder et al., (1992) Gene 110(1):89-94
<u></u>	СВ	Yao et al., (1992) PCR Methods Appl <u>1</u> (3):205-207
	СС	Atreya et al (1992) Plant Mol Biol. 19(3):517-522
	CD	Zoller et al., (1992) Curr Opin Biotechnol. <u>3</u> (4):348-354
	CE	Heda et al., (1992) Nucleic Acid Res. <u>20</u> (19):5241-5242
	CF	Horton et al., (1993) Methods Enzymol <u>217</u> :270-279
	CG	The whys and wherefores of DNA amplification. Biotechnology (NY). 1993 Aug; 11(8):940-942
	СН	Clackson et al., (1991) Nature <u>352</u> (6336)624-628
	CI	Smith et al., (1993) PCR Methods Appl. <u>2</u> (3):253-257
	CJ	Weisberg et al., (1993) Biotechniques <u>15</u> (1):68-70, 72-4, 76.
	СК	Marks, et al., (1991) J Mol Biol <u>222(3):581-597</u>
	CL	Harlow et al., (1994) Methods Mol Biol <u>31</u> :87-96
	СМ	Yon et al., (1989) Nucleic Acids Res. <u>17</u> (12)4895
	CN	Ho et al., (1990) DNA & Prot. Engineer. Tech. 2:50-55
	СО	Horton et al., (1990) Biotechniques 8(5):528-535
	СР	Osuna et al. (1991) Gene. <u>106</u> :7-12
	CQ	Dube et al. (1991) Biochemistry <u>30(51):11760-7</u>
	CR	Ghosh et al., (1991) Biochem <u>30</u> :11767-74
	cs	Paabo et al., (1990) J Biol Chem <u>265(8):4718-4721</u>

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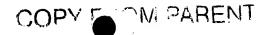
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СТ	Sambrook et al., (1989) Molecular cloning, A Labroratory Manual, 2 nd Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York.	
CU	Opposition by Diversa Corporation filed in the matter of Australian Application 703264 Affymax Technology NV, September 23, 1999.	·

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Filing Date	December 18, 1996 Undssigned			
First Named Inventor	Phillip A. Patten			
Group Art Unit	1634			
Examiner Name	Zitomer, S.			
Attorney Docket Number	02 020500U3 02-020522US			

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First Named Inventor	<u> </u>
Group Art Unit	1634
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NO.	WO	89/06694	A1	Trustees of the University of Pennsylvania	07-27-89	Page 5, lines 8-36; page 7, lines 16-27; page 9, lines 6-16	
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Application Number	08/769,002 massignel
Filing Date	December 18, 1996 Wassian
First Named Inventor	Phillip A. Patten
Group Art Unit	1634
Examiner Name	Zitomer, S.
Attorney Docket Number	02 020500US OL-010572US

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		JONES, ET AL., DNA Mutagenesis and Recombination. Nature. April 19, 1990, pages 793-794, Vol. 344,							
		PRODROMOU et al., PROTOCOL: Recursive PCR: a novel technique for total gene synthesis, Protein Engineering, 1992, pages 827-829, Vol. 5, No. 8. Oxford University Press,							
		BENDIXEN, et al. A Yeast Mating-Selection Scheme for Detection of Protein-Protein Interactions. Nucleic Acids Research, 1994, pages 1778-1779, Vol. 22, No. 9,							
		MANDECKI, et al, Fokl method of gene synthesis (Recombinant DNA; oligodeoxyribonucleotide; bridge mutagenesis; cloning; gene assembly; HIV) Gene. 1988. Pages 101-107, Vol. 68, Elsevier Science Publishers							
		REISKOFSKI et al., Polymerase Chain Reaction (PCR) Techniques for Site-Directed Mutagenesis. Biotech. Adv. 1992, pages 535-547, Vol. 10, Pergamon Press, Ltd, Great Britain							

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^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)			•			
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Examiner Initial	Document No.	Date	Name	Class	Sub-class	Filing Da
AA	5,824,485	10/20/98	Thompson et al.			
AB	5,783,431	7/21/98	Peterson et al.			
AC	5,629,179	5/13/97	Mierendorf et al.			
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AH	WO 98/28416	7/2/98	PCT		<u> </u>	- 86 - 68
AI	WO 98/01581	1/15/98	PCT			
AJ	WO 97/35966	10/2/97	PCT			
AK	WO 97/25410	7/17/97	PCT			
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AN	Marton et al., "D	NA Nicking Favor	s PCR Recombination", Nuc	leic Acids Kes., 19(-1 12.423 455	(1004)
AO	Winter et al., "M	aking Antibodies I	By Phage Display Technolog	y", Ann. Kev. Immu	<u>noi.</u> , 12:433→33 (ode in
AP Greener et al., "An Efficient Random Mutagenesis Technique Using An E. coli Mutator Strain", Methods in Molecular Biology, 57:375-385 (1995)						

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

DATE CONSIDERED

PA 183705 v1

EXAMINER

Attorney Docket No.: 1809 22 0205 22 Application No.: 08.621.57 FORM PTO-1449 (Modified) Applicant: Stemmer et al. LIST OF PATENTS AND PUBL APPLICANT'S INFORMATION DISCLOSURE Filing Date: March 25, 1996 Group: 1634 STATEMENT (Use several sheets if necessary) U.S. PATENT DOCUMENTS P_~: Reference Designation Sub-class Filing In Class Name Document No. Date **Examiner Initial** (PADO N A Amold et al. 5,316,935 05/31/94 AA s 16 Stemmer et al. 5,834,252 11/10/98 AB 28 Minshull et al. 11/17/98 5,837,458 AC FOREIGN PATENT DOCUMENTS Transier C Sub-class Class Date Country Document No. (Yes N **PCT** 05/30/91 WO 91/07506 AD COPY FROM PARENT **PCT** 10/17/91 WO 91/15581 ΑE **PCT** 10/31/91 WO 91/16427 AF **PCT** WO 95/22625 08/24/95 AG **PCT** WO 96/33207 10/24/96 ΑH OTHER ART (Including Author, Title. Date, Pertinent Pages. Etc.) Balint et al., "Antibody Engineering By Parsimonious Mutagenesis", Gene, 137(1):109-118 (1993) ΑI Bartel et al., "Isolation of New Ribozymes From a Large Pool of Random Sequences", Science, 261:1411-1413 ΑJ (1993)Crameri et al., "Combinatorial Multiple Cassette Mutagenesis Creates All The Permutations Of Mutant And ΑK Wild-Type Sequences", Biotechniques, 18(2):194-196 (1995) Crameri et al., "Improved Green Fluorescent Protein By Molecular Evolution Using DNA Shuffling", Nat. AL Biotechnol., 14(3):315-319 (1996) (previously submitted) Crameri et al., "Construction And Evolution Of Antibody-Phage Libraries By DNA Shuffling", Nat. Med. AM 2(1):100-102 (1996) (previously submitted) Crameri et al., "Molecular Evolution Of An Arsenate Detoxification Pathway By DNA Shuffling", Nat. AN Biotechnol., 15(5):436-438 (1997) Crameri et al., "DNA Shuffling Of A Family Of Genes From Diverse Species Accelerates Directed Evolution". AO Nature, 391(3664):288-291 (1998) Gates et al., "Affinity Selective Isolation Of Ligands From Peptide Libraries Through Display On A Lac Repressor 'Headpiece Dimer'", J. Mol. Biol., 255(3):373-386 (1996) Epreviously submitted AP Gram et al., "In Vitro Selection and Affinity Maturation of Antibodies From a Naïve Combinatorial AQ Immunoglobulin Library", Proc. Natl. Acad. Sci. USA, 89:3576-3580 (1992) Near, "Gene Conversion Of Immunoglobulin Variable Regions In Mutagenesis Cassettes By Replacement PC. AR Mutagenesis", Biotechniques. 12(1):88-97 (1992) Perlak, "Single Step Large Scale Site-Directed In Vitro Mutagenesis Using Multiple Oligonucleotides", Nucleic AS Acids Res., 18(24):7457-7458 (1990) Stemmer, "Searching Sequence Space", Biotechnology, 13:549-553 (1995) (previously Sub mitted) ΑT Stemmer et al., "Single-Step Assembly Of A Gene And Entire Plasmid From Large Numbers Of Oligodeoxyribonucleotides". Gene, 164(1):49-53 (1995) (previously Submitted) AU Stemmer, "The Evolution of Molecular Computation", Science, 270(5241):1510 (1995) (previously submitted ΑV Stemmer, "Sexual PCR and Assembly PCR" Encyclopedia Mol. Biol., VCH Publishers, New York, pp. 447-257 AW (1996)Weber et al., "Formation of Genes Coding for Hybrid Proteins by Recombination Between Related, Cloned Grees AXin E. Coli," Nucleic Acids Research, 11(16):5661-5669 (1983) Weisberg et al., "Simultaneous Mutagenesis Of Multiple Sites: Application Of The Ligase Chain Reaction U=2 AY PCR Products Instead Of Oligonucleotides", BioTechniques, 15(1):68-76 (1993)

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i httik Wi h i ()-1449 (Mioditica)		Attorney Docket No.: \$809 CO - 0207200 Applicant: Stemmer et al.	Application No.: 08/621,8:3-		
ADDITICANT'S	INFORMATION DISCLOSURE	Filing Date: March 25, 1996	Group: 1634		
A 7	AZ Zhang et al., "Directed Evolution Of A Fucosidase From A Galactosidase By DNA Shuffing And Screening 1997 Not. Acad. Sci. USA, 94(9):4504-4509 (1997)				
BA	Zhao et al., "Molecular Evolution Biotech., 16:258-261 (1998)	by Staggered Extension Process (StEP) In Vitro	Recombination", <u>Nature</u>		
EYAMINER		DATE CONSIDERED			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and net considered. Include copy of this form with next communication to applicant.

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AA	5,830,721	11/03/98	Stemmer et al.			· · · · · · · · · · · · · · · · · · ·
AB	5,811,238	09/22/98	Stemmer et al.			F-6-0
AC	5,763,192	06/09/98	Kauffman et al.			% S = 5
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FORM PTO-1449 (Modified)

Attorney Docket 018097-014612US Serial No.:

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LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT

(Use several sheets if necessary)

EXAMINER.

Applicant: Stemmer and Crameri

Group: Filing Date:

*2*9807 March 25, 1998 CWQ58x U.S. PATENT DOCUMENTS Reference Designation Filing Late Class Sub-Name Date Document No. Examiner (If class Initial Appropriate; Goodman et al. 02/19/91 4,994,368 AA CORY FHOM PARENT Hartley 08/27/91 AB 5,043,272 03/03/92 Gray 5,093,257 AC Goeddel et al. 06/29/93 5,223,408 AD Wu 01/18/94 5,279,952 AE 9/6 Prasher 12/01/94 5,360,728 AF Khosla et al 05/28/96 5,521,077 AG Prasher 07/30/96 5,541,309 AH 02/25/97 Stemmer 5,605,793 AI Grandi et al. 07/29/97 5,652,116 AJ FOREIGN PATENT DOCUMENTS Translation Class Sub-Country Date Document No. (yes/== class 01/13/88 Europe EP 252666 B1 AK PCT 07/12/90 WO 90/07576 AL PCT 02/07/91 WO 91/01087 AM PCT 06/29/95 WO 95/17413 AN PCT 02/27/97 WO 97/07205 AO OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.) Arkin et al., "An algorithm for protein engineering: Stimulation of recursive ensemble mutagenesis" Proc. Natl. Acad. Sci. USA 89:7811-7815 (1992). AP Beaudry et al., "Directed evolution of an RNA enzyme" Science 257:635-641 _ AO (1992).Berger et al. "Phoenix mutagenesis: One-step reassembly of multiply cleaved AR plasmids with mixtures of mutant and wild-type fragments" Anal. Biochem. 214:571-579 (1993). DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line throug citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449 (Modified) LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)		Attorney Docket	Serial No.: 08/621,859 UNO	isagnia	
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AS	Berkhout et al. "In vivo sele Nucleic Acids Res. 21:5020-50	ection of randomly mutated 023 (1993).	retroviral geno	mes"	
AT	Cadwell et al. "Randomization Applications 2:28-33 (1992).	of genes by PCR mutagenes (previously Submitted	sis" <u>PCR Methods</u>)	and	
AU	Calogero et al. "In vivo reco Microbiol. Lett. 97:41-44 (19		ion of hybrid gen	les"	
AV	Caren et al. "Efficient sampl Biotechnology 12:517-520 (199	ing of protein sequence sp 4).	pace for multiple	mutatts"	
AW	Delagrave et al. "Recursive ensemble mutagenesis" Protein Engineering 6:327-331 (1993).				
AX	Feinberg and Vogelstein "A technique for radiolabeling DNA restriction endonuclease fragments to high specific activity" Anal. Biochem. 132:6-13 (1983).				
AY	Heim et al. "Wavelength mutati fluorescent protein" Proc. Nat	ions and postranslational a <u>cl. Acad. Sci. USA</u> 91:1250	autoxidation of 9 1-12504 (1994).	green	
AZ	Hermes et al. "Searching sequence space by definably random mutagezesis: Improving the catalytic potency of an enzyme" Proc. Natl. Acad. Sci. USA 87:696-700 (1990).				
AAA	Ho et al. "Site-directed mutagenesis by overlap extension using the polymerase chain reaction" Gene 77:51-59 (1989).				
AAB	Horton et al. "Engineering hybrid geneswithout the use of restriction enzymes: Gene splicing by overlap extension" Gene 77:61-68 (1989).				
AAC	Jones et al. "Recombinant cicle PCR and recombination PCR for site-specific mutagenesis without PCR product purification" <u>BioTechniques</u> 12:528-530, 532, 534-535 (1992).				
AAD	Kim et al. "Human immunodeficiency virus reverse transcriptase" J. Biol. Chen. 271:4872-4878 (1996).				
AAE	Leung et al. "A method for ra modified polymerase chain rea	andom mutagenesis of a definition" <u>Techniques</u> 1:11-15	ined DNA sequent (1989).	usirş a	
EXAMINER	DATE C	ONSIDERED			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPF 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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AAF	Marks et al. " by chain shuff	By-passing imm ling" <u>Bio/Tech</u>	unization: Building high a nology 10:779-782 (1992).	ffinity human an	tibosies	
AAG	Meyerhans et al. "DNA recombination using PCR" Nucleic Acids Res. 18:1687-1691 (1990).					
AAH	Oliphant et al. "Cloning of random-sequence oligodeoxynucleotides" <u>Gene</u> 44:177-183 (1988).					
AAI	Pharmacia Catalog pp. 70-71 (1993 Edition).					
AAJ	Pompon et al. "Protein engineering by cDNA recombination in yeasts: Shuffling of mammalian cytochrome P-450 functions" Gene 83:15-24 (1989).					
AAK	Reidhaar-Olson oinformational co	et al. "Combina ontent of prote	atorial cassette mutagenes ein sequences" Science 241	is as a probe of :53-57 (1988).	the	
AAL	Rao et al. "Reco	ombination and prome mosaic vi	polymerase error facilita irus" <u>J. Virol.</u> 67:969-979	te restoration of (1993).	E	
AAM	linker library p	prepared by ena	an active single chain Fv a zymatic inverse PCR" <u>BioTe</u>	<u>chniques</u> 14:256-2		
AAN	Stemmer et al. "Rapid evolution of a protein in vitro by DNA shuffling" Nature 370:389-391 (1994). (previously Submiffed)					
AAO	Stemmer et al. "DNA shuffling by random fragmentation and reassembly: In vitro recombination for molecular evolution" <u>Proc. Natl. Acad. Sci. USA</u> 91:10747-10751 (1994). (previously Submitted)					
DYAMINDD		DATE C	ONSIDERED			

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicanc.

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FORM PTO-1449 (Modified)

LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE

STATEMENT (Use several sheets if necessary) Attorney Docket No.

Serial No.: 18097-02050002-020522U\$ 08/769,062 UNUSG

Applicant: PHILLIP A. PATTEN et al.

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Reference	Designation		U.S. PATENT DOCUMENTS			
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AA	3,817,837	06/18/74	Rubenstein et al.	195		
AB	3,850,752	11/26/74	Schuurs et al.	G01N 31	14	PT C
AC	3,939,350	02/17/76	Kronick et al.	G01T 1	20	S. S.
AD	3,996,345	12/07/76	Ullman et al.	G01N 21	00	95.
AE	4,275,149	06/23/81	Litman et al.	B12Q 1	66	0.50
AF	4,277,437	07/07/81	Maggio	G01N 33	54	J. =
AG	4,366,241	12/28/82	Tom et al.	G01N 33	54	
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AS			ller's ratchet decrease . Sci. U.S.A. 93:906-90		a DNA-b	ased
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AU	Barnes, W.M., yield from λ 2220 (1994)	"PCR amplifi bacteriophage	cation of up to 35-kb D templates," <u>Proc. Natl</u>	ONA with high Acad. Sci.	fidelit U.S.A.	y and high 91:2216-
AV	Barry, M.A. e cell-binding Med. 2(3):299	peptides from	d cell-targeting gene t random peptide-present	herapy vector ing phage lib	s: Sel raries,	ection of " <u>Nacure</u>

Attorney Docket No. Serial No.: FORM PTO-1449 (Modified) 08/768,062 massigned 18097 020500 OZ~020522US LIST OF PATENTS AND PUBLICATIONS FOR Applicant: PHILLIP A. PATTEN et al. APPLICANT'S INFORMATION DISCLOSURE (Use several sheets if necessary) Filing Date: 12/18/96 Group: Unknown Benka, M.L. et al., "The thrombin receptor in human platelets is coupled with _ AW GTP binding protein of the Ga, family, "FEBS Letts. 363:49-52 (1995) Berek, C. et al., "Mutation Drift and Repertoire Shift in the Maturation Immune Response," Immunological Reviews 96:23-41 (1987) _ AX Bird, R.E. et al., "Single-Chain Antigen-Binding Proteins," Science 242:423-425 _ AY (1988)Broach, J.R. et al., "High-throughput screening for drug discovery," Nature _ AZ Supp. 384:14-16 (1996) _ BA Cadwell, R.C. et al., "Randomization of Genes by PCR Mutagenesis," PCR Methods and Applications 2:28-33 (1992) Cantwell, C.A. et al., "Cloning and expression of a hybrid Streptomyces BB clavuligerus cef E gene in Peniciilium chrysogenum, " Curr. Genet. 17:213-221 (1990) _ BC Chen, C.C.H. et al., "Structure of a Phosphonate-inhibited β -Lactamase, Analog of the Tetrahedral Transition State/Intermediate of β -Lactam Hydrolysis," J. Mol. Biol. 234:165-178 (1993) Chen, K. et al., "Tuning the activity of an enzyme for unusual environments; BD Sequential random mutagenesis of subtilisin E for catalysis in dimethylformamide, "Proc. Natl. Acad. Sci. U.S.A., 90:5618-5622 (1993) __ BE Chong, S. et al., "Protein Splicing Involving the Saccharomyces cerevisiae VMA Intein, " J. Biol. Chem. 271(36):22159-22168 (1996) Courtney, L.P. et al., "An anti-IL-2 antibody increases serum halflife and __ BF improves anti-tumor efficacy of human recombinant interleukin-2," Immunopharmacology 28:223-232 (1994) Crameri, A. et al., "Construction and evolution of antibody-phage libraries by BG DNA shuffling, " Nature Medicine 2(1):100-102 (1996) ___ вн Crameri, A. et al., "Improved Green Fluorescent Protein by Molecular Evolution Using DNA Shuffling, "Nature Biotech. 14:315-319 (1996) Dangl, J.L. et al., "Rapid Isolation of Cloned Isotype Switch variants Using BI Fluorescence Activated Cell Sorting, "Cytometry 2(6):395-401 (1982) Dierick, H. et al., "Incorporation of DITP or 7-deaza dGTP during PCR improves _ BJ sequencing of the product, "Nucl. Acids Res. 21(18):4427-4428 (1993) Duncan, R. et al., "Polymer Conjugates, Pharmacokinetic Considerations for __ BK Design and Development," Clin. Pharmacokinet. 27(4):290-306 (1994) Dunn, I.S., "Assemby of Functional Bacteriophage Lambda Virions Incorporating C-BL Terminal Peptide or Protein Fusions with the Major Tail Protein, " J. Mol. Biol. 248:497-506 (1995) Fish, E.N. et al., "Human Leukocyte Interferon Subtypes have Different BM Antiproliferative and Antiviral Activies on Human Cells, " Biochem. Biophys. Res. Commun. 112(2):537-546 (1983) Gascoigne, N.R.J. et al., "Secretion of a chimeric T-cell receptor-_ BN immunoglobulin protein, "Proc. Natl. Acad. Sci. U.S.A. 84:2936-2940 (1987) Gates, C.M. et al., "Affinity Selective Isolation of Ligands from Peptide BO Libraries Through Display on a lac Repressor 'Headpiece Dimer' " J. Mol. Biol.

255:373-386 (1996)

Attorney Docket Serial No.: FORM PTO-1449 (Modified) 18097 08/769,062 Unassian 0,5025572 LIST OF PATENTS AND PUBLICATIONS FOR Applicant: PHILLIP A. PATTEN et al. APPLICANT'S INFORMATION DISCLOSURE Filing Date: 12/18/96 **STATEMENT** (Use several sheets if necessary) Group: Unknown ___ BP Gram, H. et al., "Phage display as a rapid gene expression system: prodution of bioactive cytokine-phage and generation of neutralizing monoclonal antibodies," J. Immunological Methods 161:169-176 (1993) Hartl, F.U., "Molecular chaperones in cellular protein folding," Nature 381:571-_ BQ 580 (1996) Higazi, A.A et al., "Single-Chain Urokinase-Type Plasminogen Activator Bound to BR its Receptor is Relatively Resistant to Plasminogen Activator Inhibitor Type 1," Blood 87(9):3545-3549 (1996) Hogan, J.C., "Directed combinatorial chemistry," Nature Supp. 384:17-19 (1996) BS _ BT Holskin, B.P. et al., "A Continuous Fluorescence-Based Assay of Human Cytomegalovirus Protease Using a Peptide Substrate, "Anal. Biochem. 226:148-155 (1995)Horisberger, M.A. et al., "Interferon-Alpha Hybrids," Pharmac. Ther. 66(3):507-BU 534 (1995) Hu, R. et al., "Evidence for Multiple Binding Sites for Several Components of BV Human Lymphoblastoid Interferon- α , <u>J. Biol. Chem.</u> 268(17):12591-12595 (1993) __ BW Janda, K.D. et al., "Direct selection for a catalytic mechanism from combinatorial antibody libraries, " Proc. Natl. Acad. Sci. U.S.A. 91:2532-2536 (1994)BX Kang, Y.S. et al.,. "Effects of Expression of Mammalian $G\alpha$ and Hybrid Mammalian-Yeast Ga Proteins on the Yeast Pheromone Response Signal Transduction Pathway," Mol. Cell Biol. 10(6):2582-2590 (1990) Khosla, C. et al., "Generation of polyketide libraries via combiantorial _ BY biosynthesis, " TIBTECH 14 (1996) __ BZ Kim, B. et al., "Human immunodeficiency virus reverse trascriptase substitutes for DNA polymerase I in Escherichia coli, "Proc. Natl. Acad. Sci. U.S.A. 92:684-688 (1995) Kirpekar, F. et al., "7-Deaza Purine Bases Offer a Higher Ion Stability in the _ CA Analysis of DNA by Matrix-assisted Laser Desorption/Ionization Mass Spectrometry, " Rapid Communications in Mass Spectrometry 9:525-531 (1995) _ CB Kontsek, P., "Human Type I Interferons: Structure and Function," Acta <u>Virologica</u> 38:345-360 (1994) Kristensen, C. et al., "A single-chain insulin-like growth factor I/insulin __ CC hybrid binds with high affinity to the insulin receptor," Biochem. J. 305:981-986 (1995) Langer, J.A. et al., "Binding of Human Alpha-Interferons to Natural Killer _ CD Cells, J. Interferon Res. 6:97-105 (1986) Lathrop, R.H. et al., "Global Optimum Proetin Threading with Gapped Alignment CE and Empirical Pair Score Functions, " J. Mol. Biol. 255:641-665 (1996) Levichkin, I.V. et al., "A New Approach to Construction of Hybrid Genes: __ CF Homolog Recombination Method, Mol. Biol. 29(5):572-577 (1995) __ CG Li, J. et al., "Single Chain Human Interleukin 5 and Its Asymmetric Mutagenesis for Mapping Receptor Binding Sites, " J. Biol. Chem. 271(4):1817-1820 (1996) Lotze, M.T. et al., "High-Dose Recobinant Interleukin 2 in the Treatment of CH Patients with Disseminated Cancer, " J. Amer. Med. Assoc. 256(22):3117-3124

(1986)

FORM PTO-	1449 (Modified)	Attorney Docket No.	Serial No.: 0 8/769,062 WASSIGNE		
APPLICANT	ATENTS AND PUBLICATIONS FOR 'S INFORMATION DISCLOSURE	Applicant: PHILLIP A. P.	•		
STATEMENT (Use severa	l sheets if necessary)	Filing Date: 12/18/96	Group: Unknown		
CI	Lundberg, K.S. et al., "High polymerase isolated from Pyr	-fidelity amplification ococcus furiosus," <u>Gene</u> 1	using a thermostable DNA .08:1-6 (1991)		
CJ	Mattheakis, L. C. et al., "As ligands from very large pept: 91:9022-9026 (1994)	s <i>in vitro</i> polysome d is pl ide libraries," <u>Proc. Nat</u>	ay system for identifying l. Acad. Sci. U.S.A.		
ск	Matthews, D.J. et al., "Subst Monovalent Phage Display," So				
CL	McCafferty, J. et al., "Select Fragments That Bind a Transit Biochem. Biotech. 47:157-173	ion-State Analog by Phage	ion of Murine Antibody e Display," <u>Applied</u>		
CM	Medberry, S.L. et al., "Intra site-specific recombination,"				
CN	Meister, A. et al., "Biologica Recombinant Interferons and th	al Activities and Recepto heir Hybrids," <u>J. Gen. Vi</u>	r Binding of Two Human <u>rol.</u> 67:1633-1643 (1986)		
co	Metcalf, W.W. et al., "Mutation Operon for Phosphonate Degrada 175(11):3430-3442 (1993)				
CP	Northrup, J.P. et al., "Characterization of the Nuclear and Cytoplasmic Components of the Lymphoid-specific a Nuclear Factor of Activated T Cells (NF-AT) Complex," J. Biol. Chem. 268(4):2917-2923 (1993)				
cō	Nürnberg, B. et al., "Receptor transmembrane signal transduct	es and G proteins as primation," <u>J. Mol. Med.</u> 73:12:	ary components of 3-132 (1995)		
CR	Ohnishi, H. et al., "Prolongat Augmentation of Lymphokine-act Canc. Res. 50:1107-1112 (1990)	ivated Killer Cell Activ:	F Interleukin 2 and ity by Pepstatin in Mice,"		
cs	O'Neil, K.T. et al., "Phage di evolution," <u>Curr. Op. Struct.</u>	splay: protein engineer: Biol. 5:443-449 (1995)	ing by directed		
СТ	Ortaldo, J.R. et al., "A speci boost human natural killer act (1984)	es of human α interferon ivity," <u>Proc. Natl. Acad</u>	that lacks the ability to Sci. U.S.A. 81:4926-4929		
cu	Overall, M.L. et al., "Differe Surface of Epithelial and Lymp	ent Interactions of Inter phoid Cells," <u>J. Interfer</u>	feron-α Subtypes at the on Res. 12:281-288 (1992)		
cv	Ozes, O.N. et al., "A Comparis Interferons- α : Antiviral, Ant Activities," J. Interferon Res	ciproliferative, and Natu	th Natural Recombinant ral Killer-Inducing		
CW	Panka, D.J. et al., "Variable or increased affinity of varia Sci. U.S.A. 85:3080-3084 (1988)	ant anti-digoxin antibodi	nces result in decreased es," <u>Proc. Natl. Acad.</u>		
сх	Papas, T.S. et al., "Nucleotic Region and Large Terminal Redu <u>Cell. Biochem.</u> 20:95-103 (1982	undancies (LTR) of Avian	ion of the Transforming Myeloblastosis (AMV)," <u>J.</u>		
CY	Parker, L.T. et al., "Peak He: Products Using Taq Dye-Termina	ight Variations in Automa ator Chemistry," <u>BioTechn</u>	ted Sequencing of PCR iques 19(1):116-121 (1995)		
CZ	Patten, P.A. et al., "The Immo 271:1086-1091 (1996)	unological Evolution of C	atalysis," <u>Science</u>		

FORM PTO-	-1449 (Modified)	Attorney Docket No.	Serial No.: 08/769,062 MASS 4MOS		
	PATENTS AND PUBLICATIONS FOR	Applicant: PHILLIP A. P.	<i>[</i> 1] '		
STATEMENT (Use severa	l sheets if necessary)	Filing Date: 12/18/96	Group: Unknown		
DA	Pérez-Pérez, J. et al., "Inc Escherichia coli," <u>Biotechno</u>	reasing the Efficiency of logy 12:178-180 (1994)	Protein Export in		
DB	Pérez-Pérez, J. et al., "DNAK/DNAJ Supplementation Improves the Periplasmic Production of Human Granulocyte-Colony Stimulating Factor in Escherichia coli," Biochem. Biophys. Res. Commun. 210(2):524-529 (1995)				
DC	Post, G.R. et al., "G protein regulating growth responses,"	n-coupled receptors and s FASEB J. 10:741-749 (19:	ignaling pathways 96)		
DD	Price, L.A. et al., "Function the Yeast Pheromone Response	nal Coupling of a Mammalia Pathway," <u>Mol. Cell Biol.</u>	an Somatostatin Receptor to _ 15(11):6188-6195 (1995)		
DE	Pugsley, A.P., "The Complete Bacteria," <u>Microbiol. Rev.</u> 57	General Secretory Pathway	n in Gram-Negative		
DF	Ranu, R.S., "DNA Sequencing w 395 (1995)	ith $\Delta Taq^{ exttt{0}}$ DNA Polymerase,	" <u>BioTechniques</u> 18(3):390-		
DG	Raport, C.J. et al., "The orphan G-protein-coupled receptor-encoding gene V28 is closely related to genes for chemokine receptors and is expressed in lymphoid and neural tissues," Gene 163:295-299 (1995)				
DH	Rashtchian, A., "Novel methods for cloning and engineering genes using the polymerase chain reaction," <u>Current Op Biotech.</u> 6:30-36 (1995)				
DI	Reisine, T. et al., "Molecular Proteins and Effector Systems,	Mechanisms of Opiate Red " <u>Annals N.Y. Acad. Sci.</u>	ceptor Coupling to G 780:168-175 (1996)		
DJ	Rohlmann, A. et al., "Sustaine Cre recombinase," <u>Nature Biote</u>				
DK	Rosenberg, A.H. et al., "Effect Escherichia coli, Demonstrated Bacteriology 175(3):716-722 (1	l with a Versatile Codon 1	dons on Translation in Test System," <u>J.</u>		
DL	Saggio, I. et al., "Functional <u>Gene</u> 152:35-39 (1995)	phage display of ciliary	neurotrophic factor,"		
DM	Sandkvist, M. et al., "Secreti bacteria," <u>Current Op. Biotech</u>	on of recombinant proteir	ns by Gram-negative		
DN	Sauer, B. et al., "Site-specific DNA recombination in mammalian cells by the Cre recombinase of bacteriophage P1," Proc. Natl. Acad. Sci. U.S.A. 85:5166-5170 (1988)				
DO	Schatz, P.J. et al., "Genetic Analysis of Protein Export in Escherichia coli," Ann. Rev. Genet. 24:215-248 (1990)				
DP	Scheidl, T.M. et al., "Automated Fluorescent Dye-Terminator Sequencing of G+C-Rich Tracts with the Aid of Dimethyl Sulfoxide," <u>Biotechniques</u> 19:691-694 (1995)				
DQ	Seed, B. et al., "Molecular cl receptor, by a rapid immunosel 84:3365-3369 (1987)	loning of the CD2 antigen lection procedure," <u>Proc.</u>	, the T-cell erthyrocyte Natl. Acad. Sci. U.S.A.		
DR	Seed, B., Developments in expr (1995)	ression cloning," <u>Current</u>	Op. Biotech. 6:567-573		
DS	Seto, D. et al., "DMSO resolve fluorescent dye labeled prime:	es certain compressions a r-based DNA sequencing re	nd signal dropouts in actions," <u>DNA Sequence</u>		

Shenker, A., "G Protein-coupled receptor structure and function: the impact of disease-causing mutations," Baillieres Clin. Endo. Metab. 9(3):427-451 (1995)

DT

5:131-140 (1995)

Serial No.: Attorney Docket FORM PTO-1449 (Modified) 18097-020500 08/769,062 UNASSIAN 01-0105-22-05 LIST OF PATENTS AND PUBLICATIONS FOR Applicant: PHILLIP A. PATTEN et al. APPLICANT'S INFORMATION DISCLOSURE Filing Date: 12/18/96 STATEMENT (Use several sheets if necessary) Group: Unknown Siderovski, D.P. et al., "A new family of regulators of G-protein-coupled __ DU receptors?" Current Biology 6(2):211-212 (1996) Simonen, M. et al., "Protein Secretion in Bacillus Species," Microbiol. Rev. _ DV 57(1):109-137 (1993) Skatrud, P.L. et al., "Genetic engineering of β -lactam antibiotic biosynthetic _ DW pathways in filamentous fungi, "TIBTECH 10:324-329 (1992) Skerra, A. et al., "Filter Screening of Antibody Fab Fragments Secreted from _ DX Individual Bacterial Colonies: Specific Detection of Antigen Binding with a Two-Membrane System, " Anal. Biochem. 196:151-155 (1991) Smirnov, Y.V. et al., "Synthesis in Escherichia coli and a Rapid Method of _ DY Isolating High-Activity Recombinant His, DNA Polymerase from Thermus aquaticus, " Russian J. Bioorganic Chem. 21(5):341-342 (1995) Smith, L.M., "Sequence from spectrometry: A realistic prospect," Nature _ DZ Biotechnology 14:1084-1087 (1996) Smith, R.A.G. et al., "Chemical derivatization of therapeutic proteins," TIBTECH 11:397-403 (1993) Solar, I. et al., "Linker modification introduces useful molecular instability EB in a single chain antibody, " Protein Engineering 8(7):717-723 (1995) Song, Z.H. et al., "Molecular Cloning and Chromosomal Localization of Human EC Genes Encoding Three Closely Related G Protein-Coupled Receptors, " Genomics 28:347-349 (1995) Spiegel, A.M., "Defects in G Protein-Coupled Signal Transduction in Human ED Disease, " Ann. Rev. Physiol. 58:143-170 (1995) Spiegel, A.M., "Genetic Bases of Endocrine Disease," J. Clin. Endocrin. Metab. __ EF 81(7):2434-2442 (1996) Stemmer, W.P.C., "Rapid evolution of a protein in vitro by DNA shuffling," EG Nature 370:389-391 (1994) Stemmer, W.P.C., "DNA shuffling by random fragmentation and reassembly: In _ EH vitro recombination for molecular evolution, " Proc. Natl. Acad. Sci. U.S.A. 91:10747-10751 (1994) Stemmer, W.P.C., "Searching Sequence Space, Using recombination to search more __ EI efficiently and thoroughly instead of making bigger combinatorial libraries, " Biotechnology 13:549-553 (1995) Stemmer, W.P.C. et al., "Single-step assembly of a gene and entire plasmid from EJ large numbers of oligodeoxyribonucleotides, " Gene 164:49-53 (1995) Stemmer, W.P.C., "The Evolution of Molecular Computation," Science 270:1510 _ EK (1995)Strader, C.D. et al., "The family of G-protein-coupled receptors," FASEB J. EL 9:745-754 (1995) Sweasy, J.B. et al., "Detection and characterization of mammalian DNA polymerase EM β mutants by functional complementation in Escherichia coli, " Proc. Natl. Acad. Sci. U.S.A. 90:4626-4630 (1993) Sweasy, J.B. et al., "DNA Polymerase β Can Substitute for DNA Polymerase I in EN the Initiation of Plasmid DNA Replication, " J. Bacteriology 177 (10:2923-2925

(1995)

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FORM PTO-	-1449 (Modified)	Attorney Docket	Serial No.:			
APPLICANT	PATENTS AND PUBLICATIONS FOR T'S INFORMATION DISCLOSURE	Applicant: PHILLIP A.	۸			
STATEMENT (Use severa	l sheets if necessary)	Filing Date: 12/18/96	Group: Unknown			
EO	Su, S.S. et al., "Escherichi base pairs," Proc. Natl. Aca	Su, S.S. et al., "Escherichia coli mutS-encoded protein binds to mismatched DNA base pairs," Proc. Natl. Acad. Sci. U.S.A. 83:5057-5061 (1986)				
EP	Suzuki, M. et al., "Random mutagenesis of <i>Thermus aquaticus</i> DNA polymerase I: Concordance of immutable sites <i>in vivo</i> with the crystal structure," <u>Proc. Natl. Acad. Sci. U.S.A.</u> 93:9670-9675 (1996)					
EQ	Tabor S. et al., "DNA Sequence polymerase," <u>J. Biol. Chem.</u> 2	ce Analysis with a Modif 265(14):8322-8328 (1990)	ied Bacteriophage T7 DNA			
ER	Théze, J. et al., "Interleukin 2 and its receptors: recent advances and new immunological functions," Immunol. Today 17(10):481-486 (1996)					
ES	Turner, S.L. et al., "Use of Deoxyinosine in PCR to Improve Amplification of GC-Rich DNA," <u>Biotechniques</u> 19(1):48-52 (1995)					
ET	von der Osten, C. et al., "Protein engineering of subtilisins to improve stability in detergent formulations," <u>J. Biotech.</u> 28:55-68 (1993)					
EU	Wagner, R. et al., "Mutation detection using immobilized mismatch binding protein (MutS)," Nucl. Acids Res. 23(19):3944-3948 (1995)					
EV	Wall, J.G. et al., "Effects of overexpressing folding modulators on the in vivo folding of heterologous proteins in Escherichia coli," Current Op. Biotech. 6:507-516 (1995)					
EW	Weck, P.K. et al., "Comparison of the Antiviral Activities of Various Cloned Human Interferon-α Subtypes in Mammalian Cell Cultures," <u>J. Gen. Virol.</u> 57:233-237 (1981)					
EX	Wettstein, D.A., "Expression of a Class II Major Histocompatibility Complex (MHC) Heterodimer in a Lipid-linked Form with Enhanced Peptide/Soluble MHC Complex Formation at Low pH," J. Exp. Med. 174:219-228 (1991)					
EY	Young, N.M. et al., "Thermal stabilization of a single-chain Fv antibody fragment by introduction of a disulphide bond," FEBS Letts. 377:135-139 (1995)					
EZ	Zhang, T. et al., "Circular Pe 12318 (1993)	rmuation of T4 Lysozyme,	" Biochemistry 32:12311-			
FA	Zhao, X., "EPD, a novel techno 17:257-262 (1995)	ology for drug delivery,	' Adv. Drug Deliv. Rev.			
FB						
EXAMINER	DATE CO	NSIDERED				

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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FORM PTO-1449 (Modified) Attorney Docket No Serial No.: -18097-020500- 08/769,062 WURSSIA OC OWS ZZUS LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE Applicant: PHILLIP A. PATTEN et al. STATEMENT (Use several sheets if necessary) Filing Date: -12/18/96-Group: Unknown unassianed Reference Designation U.S. PATENT DOCUMENTS Examiner Document No. Date Name Class Sub-Filing Date Initial class (If Appropriate) AA 5,525,486 06/11/96 Honjo et al. C12N 15/00 AB 5,565,332 10/15/96 Hoogenboom et al. 435 69.1 AC 99. FOREIGN PATENT DOCUMENTS Document No. Date Country Class Sub-Translation class (yes/no) AD AE OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.) _ AF Cadwell et al., "RANDOMIZATION OF GENE BY PCR MUTAGENESIS" Research, PCR Methods and Applications, pp. 28-33 (1992) AG Crameri et al., "CONSTRUCTION AND EVOLUTION OF ANTIBODY-PHAGE LIBRARIES BY DNA SHUFFLING" Nature Medicine 2(1):100-102 (1996) AH Mandecki et al., "FOKI METHOD OF GENE SYNTHESIS (RECOMBINANT DNA; OLIGODEOXYRIBONUCLEOTIDE; BRIDGE MUTAGENESIS; CLONING; GENE ASSEMBLY; HIV) Gene 68:101-107 (1988) __AI Matthews et al., "SUBSTRATE PHAGE: SELECTION OF PROTEASE SUBSTRATES BY MONOVALENT PHAGE DISPLAY" Science 260:1113-1117 (1993) AJ O'Neil et al., "PHAGE DISPLAY: PROTEIN ENGINEERING BY DIRECTED EVOLUTION" Current Opinion in Structual Biology 5:443-449 (1995) _ AK Reikofski et al., "POLYMERASE CHAIN REACTION (PCR) TECHNIQUES FOR SITE-DIRECTED MUTAGENESIS" bIOTECH. aDV. 10:535-547 (1992)

DATE CONSIDERED

MINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through ation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Seed et al., "MOLECULAR CLONING OF THE CD2 ANTIGEN, THE T-CELL ERYTHROCYTE RECEPTOR, BY A RAPID IMMUNOSELECTION PROCEDURE" Proc. Natl. Acad. Sci USA

Sweasy et al., "DETECTION AND CHARACTERIZATION OF MAMMALIAN DNA POLYMERASE β MUTANTS BY FUNCTIONAL COMPLEMENTATION IN ESCHERICHIA COLI" Proc. Natl. Acad.

84:3365-3369 (1987)

Sci. USA 90:4626-4630 (1993)

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